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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/549,977 | 06/28/2006 | Vadim Iourgenko | 4-32999A | 2228 |

75074 7590 03/19/2009

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| EXAMINER | |
|---|---|
| MACFARLANE, STACEY NEE | |
| **ART UNIT** | **PAPER NUMBER** |
| 1649 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 03/19/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/549,977 | IOURGENKO ET AL. | |
| | Examiner | Art Unit | |
| | STACEY MACFARLANE | 1649 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *05 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3,4,7,9-11,13,14,17 and 19-81* is/are pending in the application.

4a) Of the above claim(s) *3,4,7,9,10,13,14,17 and 19-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 11 and 76-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Amendment*

1. Claims 1 and 11 have been amended, claims 2, 5, 6, 8, 12, 15, 16 and 18 have been cancelled, and claims 76-81 have been newly added as requested in the amendment filed on January 5, 2009. Following the amendment, claims 1, 3, 4, 7, 9-11, 13, 14, 17 and 19-81 are pending in the instant application.

Claims 3, 4, 7, 9, 10, 13, 14, 17 and 19-75 withdrawn without traverse from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Claims 1, 11 and 76-81 are under examination in the instant office action.

2. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

3. Applicant's arguments filed on January 5, 2009 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

### *Claim Rejections - 35 USC § 112*

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 11, 77, 78, 80 and 81 are rejected under 35 U.S.C. 112, second paragraph for reasons of record in the previous Office Action mailed July 3, 2008.

6. As currently amended, Claims 1, 11, 77, 78, 80 and 81 are vague and indefinite in so far as they employ the term "CREAP" as a limitation. This term is appears to be

novel in the art, and without a reference to a precise amino acid sequence identified by a proper SEQ ID NO: one of ordinary skill cannot determine the metes and bounds of "CREAP" protein(s).

7. On page 11 of Remarks filed January 5, 2009, Applicant traverses the rejection on the grounds the "CREAP" is defined within the specification as encompassing "CRE (Cyclic AMP Response Element)-activating proteins". Applicant further states that "representative examples" of proteins encompassed by the term have been provided within the specification. While this has been carefully considered it is not found persuasive to overcome the rejection for the following reasons.

8. CREAP proteins are not identified as a group of related proteins within the art and the plain meaning of "CRE (Cyclic AMP Response Element)-activating proteins" broadly encompass other proteins that are upstream of signaling, even proteins that have yet to be identified. While Applicant is entitled to be his or her own lexicographer, Applicant may rebut the broadest reasonable interpretation by clearly setting forth a definition of the term that is different from the broadest meaning. Here, Applicant has not clearly defined the metes and bounds of proteins encompassed by the term and, therefore, the rejection is maintained.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. As currently amended, Claims 1, 11, 77, 78, 80 and 81 stand as rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for reasons of record in the previous Office Action mailed July 3, 2008.

11. On pages 11-12 of Remarks (*Id*), Applicant traverses the rejection on the grounds that, by amendment, "Applicants have reduced the plenary set of "CREAP modulators" in the present claims to agents which are capable of enhancing the expression and/or activity of CREAP1". Applicant further traverses that a determination of adequate written description can include functional characteristics and "said functional characteristics of agonizing peptide mimetics of CREAP proteins are known, as they are the same functions as possessed by normally (i.e. non-pathogenically) functional CREAP proteins. These include at least an ability to activate CRE-dependent gene expression or abnormal chemokine activation" (page 12). Applicant further states,

> "Applicants also take issue with Examiner's statement at the top of page 5 of the Office Action, that "There is not even the identification of any particular portion of a structure that must be conserved for CREAP modulatory activity." When discussing agonizing peptide mimetics of CREAP proteins, as at present, the regions of conservation of said mimetics are the same regions of conservation as the CREAP proteins themselves. Said regions of conservation are described at least at the bottom of page 23, and additionally, regions of importance within the molecules are experimentally determined by the creation and usage of deletion mutants (see, e.g., Example 5, for CREAP1)."

While these arguments have been considered in full they are not found persuasive for the following reasons.

As cited as Applicant, the bottom of page 23 identifies the amino acid fragment 1-68 for CREAP1, the amino acid fragment 1-74 for CREAP2, and the amino acid fragment 1-66 for CREAP3 and Example 5 (page 60) identifies specific fragments of

CREAP1 that have functional activity, but demonstrate that even fragments containing this conserved region (1-68) are not functionally active. Furthermore, the claims broadly encompass "CREAP modulators" comprising peptide mimetics that go beyond those that are described within the specification. Furthermore, the specification fails to identify a structure-to-function correlation for those peptide fragments that serve as mimetics. It is clear from the specification that Applicant is in possession of specific peptide mimetic sequences, but the claims are not limited to these and broadly encompass a genus of molecules for which there is inadequate description. For example, the amino acid fragments of CREAP1 described on page 60 all lie within the genus of modulators encompassed by the claims, however, the data shows that only 2 out of the 5 (SEQ ID NO: 34 and SEQ ID NO: 35) have partial or full mimetic activity. This example precisely illustrates the crux of the rejection, that the claims do not require that the "modulator" possesses a particular conserved structure or distinguishing feature but that they are drawn to a genus of molecules merely described by function, and there is inadequate written description within the specification as to which of those molecules within the genus fulfill that requisite activity.

Adequate written description requires more than a mere recitation of a genus of molecules and a requisite activity as part of the invention. The compound itself is required. Therefore, the rejection is maintained.

12. As amended, Claims 1, 11 and 76-81 stand as rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, for reasons of record in the Office action mailed July 3, 2008.

On pages 12-13 of Remarks (*Id*), Applicant traverses the rejection on the grounds that the cancellations and amendments made in response to the written description rejection (above) are sufficient to overcome the enablement rejection as well. Specifically, Applicant argues that the claims no longer include inhibitors of protein activity within the scope of the instant claims, but rather at present claims employ agents that enhance or agonize protein activity and/or expression. Applicant posits that the modulators of the claims "need merely to demonstrate the same properties of CREAP1 in order to have therapeutic efficacy for the prevention, treatment, and/or amelioration of Huntington Disease." These arguments have been fully considered but are not found persuasive to overcome the rejection for the following reasons.

Claims 1, 11 and 76-81 broadly encompass methods for preventing, treating, and/or ameliorating Huntington disease comprising administering any CREAP modulator, wherein said modulator comprises one or more peptide mimetics to a CREAP protein. As stated above in sections 8 and 11 above, the broadest reasonable interpretation of the claimed method is that the term CREAP is indefinite, encompassing any Cyclic AMP Response Element-activating protein, including those that have yet to be identified. Furthermore, the modulator comprising peptide mimetics of CREAP encompasses a genus of molecules for which there is inadequate structure-to-function description within the specification. Thus, in their broadest reasonable interpretation the

claims proved for the prevention, treatment and/or amelioration the genetic disorder, Huntington's disease, by the administration of any molecule that modulates (increases or decreases) CREAP protein activity. Furthermore, it is unclear from the claims exactly which specific CREAP protein "activity" is required to be modulated in order to achieve the method (e.g. protein expression, or downstream signaling and how one assesses the modulatory effect).

The instant specification provides no guidance or direction of the method practiced with any specific modulator that upon in vivo administration was successful in the preventing, treating and/or ameliorating Huntington's chorea. Absent such guidance, one of ordinary skill in the art would rely upon what was known in the art at the time of filing with respect to CREAP protein(s) activity and Huntington's. However, even within the current literature, there is no evidence that a nexus exists between the activity of any CREAP protein and the etiology, pathology or symptomology of the genetically inherited disorder of Huntington's chorea. Therefore, there is no guidance or direction made of record that would enable a skilled artisan to be able to prevent, treat and/or ameliorate Huntington disease solely comprising administering any CREAP modulator that is one or more peptide mimetics to a CREAP protein.

Therefore, Examiner maintains that the instant specification is not enabling because one cannot follow the guidance presented therein and practice the claimed method without first making a substantial inventive contribution. In the instant case, one of ordinary skill in the art would have to first correlate CREAP protein activity with disease pathology, identify specific peptide mimetic modulators that fulfill the functional

requirements of a CREAP protein, successfully deliver them in vivo and demonstrate effective prevention, treatment and/or amelioration of Huntington Disease in order to practice the method as claimed. Such experimentation is not routine but constitutes undue experimentation in order to close the gaps between genetic inheritance, laboratory data, and clinical efficacy. Thus, the rejection is maintained.

***Conclusion***

13. No Claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is

(571)270-3057. The examiner can normally be reached on M-W and ALT F 5:30 to 3:30, TELEWORK-Thursdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
Examiner
Art Unit 1649

/John D. Ulm/
Primary Examiner, Art Unit 1649